

CLAIMS

1. Use of a multispecific antibody for the manufacture of a medicament for treating or managing an autoimmune disorder in a patient in need of such treatment or management, wherein the multispecific antibody binds to B-cell maturation antigen (BCMA) and an antigen that promotes activation of one or more T cells.
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2. The use according to claim 1, wherein the autoimmune disorder is anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE).
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3. Use of a multispecific antibody for the manufacture of a medicament for treating or managing antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in a patient in need of such treatment or management, wherein the multispecific antibody binds to BCMA and to an antigen that promotes activation of one or more T cells.
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4. The use according to any one of claims 1 to 3, wherein:
 - (a) the antigen that promotes activation of one or more T cells is selected from the group consisting of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226, preferably wherein the antigen that promotes activation of one or more T cells is CD3;
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 - (b) the multispecific antibody is a bispecific antibody that binds to BCMA and CD3; and/or
 - (c) the multispecific antibody is a bispecific antibody, optionally wherein bispecific antibody is a trivalent bispecific antibody comprising two Fab fragments of an anti-BCMA antibody, one Fab fragment of an anti-CD3 antibody, and one Fc portion, wherein the bispecific antibody is in the format BCMA Fab - Fc - CD3 Fab - BCMA Fab.
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5. The use according to any one of claims 1 to 4, wherein the multispecific antibody comprises an anti-BCMA antibody, or antigen binding fragment thereof, comprising a CDR1H, CDR2H, CDR3H CDR1L, CDR2L and CDR3L region combination selected from:

- (a) CDR1H region of SEQ ID NO:21, CDR2H region of SEQ ID NO:22, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:27, CDR2L region of SEQ ID NO:28, and CDR3L region of SEQ ID NO:20;
- 5 (b) CDR1H region of SEQ ID NO:21, CDR2H region of SEQ ID NO:22, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:25, CDR2L region of SEQ ID NO:26 , and CDR3L region of SEQ ID NO:20; or
- (c) CDR1H region of SEQ ID NO:15, CDR2H region of SEQ ID NO:16, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:18, CDR2L region of SEQ ID NO:19 , and CDR3L region of SEQ ID NO:20.
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6. The use according to any one of claims 1 to 5, wherein the multispecific antibody comprises:
- (a) an anti-BCMA antibody, or antigen binding fragment thereof, having a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:10 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:14;
- 15 (b) an anti-BCMA antibody, or antigen binding fragment thereof, having a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:10 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:13; or
- 20 (c) an anti-BCMA antibody, or antigen binding fragment thereof, having a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:9 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:11.
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7. The use according to any one of claims 1 to 6, wherein the multispecific antibody comprises an anti-CD3 antibody, or antigen binding fragment thereof, which comprises a heavy chain

- CDR1 comprising the amino acid sequence of SEQ ID NO:1, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:2, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO:3, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO:4, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO:5, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO:6.
8. The use according to claim 7, wherein the anti-CD3 antibody or antigen binding fragment thereof comprises a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:7 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:8.
9. The use according to any one of claims 1 to 3, wherein the multispecific antibody comprises a heavy and light chain set consisting of polypeptides:
- (a) SEQ ID NO:48, SEQ ID NO:55, SEQ ID NO:56, and two copies of SEQ ID NO:57;
 - (b) SEQ ID NO:48, SEQ ID NO:58, SEQ ID NO:59, and two copies of SEQ ID NO:60; or
 - (c) SEQ ID NO:48, SEQ ID NO:61, SEQ ID NO:62, and two copies of SEQ ID NO:63.
10. The use of any one of claims 1 to 9, wherein the autoimmune disease is selected from the group consisting of Systemic lupus erythematosus, IgA nephropathy, Membranous Nephropathy, Myasthenia gravis, Neuromyelitis optica, Pemphigus vulgaris, Anti-PAD4-activating rheumatoid arthritis, Sensitized / preformed antibodies in solid organ transplant, Guillain-Barre Syndrome (Acute inflammatory demyelinating polyneuropathy – AIDP), Chronic inflammatory demyelinating polyneuropathy (CIDP), Immune thrombocytopenic purpura, rheumatoid arthritis and ANCA-associated vasculitis (AAV).
11. The use according to any one of claims 3 to 10, wherein the AAV comprises diseases that are selected from the group consisting of granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA) and renal-limited ANCA-associated vasculitis.

- 5 12. The use according to any one of claims 1 to 11, wherein the autoimmune disorder (e.g. AAV) is refractory or relapsed; and/or wherein the autoimmune disorder (e.g. AAV) is newly diagnosed.
- 10 13. The use according to any one of claims 3 to 12, wherein the AAV is affecting one or more body parts of the patient selected from nervous system, eyes, nose, heart, kidneys, stomach, intestine, lungs, joints, muscles and skin.
14. The use according to any one of claims 3 to 13, wherein the AAV is generalized with presence of life- or major organ-threatening manifestations.
- 15 15. The use according to claim 14, wherein the patient has diffuse alveolar hemorrhage (DAH).
16. The use according to any one of claims 3 to 13, wherein the AAV is localized without organ-threatening manifestations.
- 20 17. The use according to any one of claims 1 to 16, wherein:
(a) the patient is in need of plasmablast reduction;
(b) the patient is at risk of developing cytokine release syndrome;
(c) the patient is at risk of developing infection;
(d) the patient is in need of induction of remission; and/or
(e) the patient is in need of maintenance of remission.
- 25 18. The use according to any one of claims 1 to 17, wherein the treatment or management results in:
(a) a reduction of plasmablasts in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or
30 100% relative to no treatment or a reference treatment;
(b) a lowered incidence of cytokine release syndrome in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment;

- (c) a lowered incidence of infection in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment;
- (d) a faster induction of remission in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment; and/or
- (e) a longer maintenance of remission in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment.
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19. The use according to claim 18, wherein the reference treatment is treatment with steroids (e.g. glucocorticoids), cyclophosphamide, an anti-CD20 monoclonal antibody (e.g. rituximab), methotrexate, azathioprine, mycophenolate, mycophenolate mofetil,
- 15 IL6R antibodies (e.g. tocilizumab, sarilumab), costimulatory blockade (e.g. abatacept), JAK inhibitors (e.g. tofacitinib, baricitinib) and/or belimumab, preferably wherein the reference treatment is treatment with steroids, cyclophosphamide or rituximab.
20. The use according to any one of claims 1 to 19, wherein the treatment or management is used for the induction of remission or the maintenance of remission.
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